

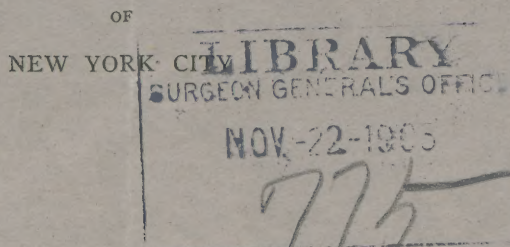
Coleman (W.) & Buxton (B. H.)

2

THE
BACTERIOLOGY OF THE BLOOD
IN
TYPHOID FEVER

BEING A REPORT ON SIXTY CASES AND A
STATISTICAL STUDY

BY
WARREN COLEMAN, M. D.
AND
B. H. BUXTON, M. D.



READ AT A MEETING OF THE NEW YORK PATHOLOGICAL SOCIETY,
FEBRUARY 10TH, 1904

(PROCEEDINGS OF N. Y. PATH. SOC., 1904, N. S. IV, P. 10)

REPRINTED FROM MEDICAL AND SURGICAL REPORT OF BELLEVUE AND ALLIED
HOSPITALS IN THE CITY OF NEW YORK, VOLUME I, 1904

THE BACTERIOLOGY OF THE BLOOD IN TYPHOID FEVER.

BEING A REPORT ON SIXTY CASES AND A STATISTICAL STUDY.*

BY WARREN COLEMAN, M. D., AND B. H. BUXTON, M. D.
OF NEW YORK CITY.

(From the Loomis Laboratory of Cornell University.)

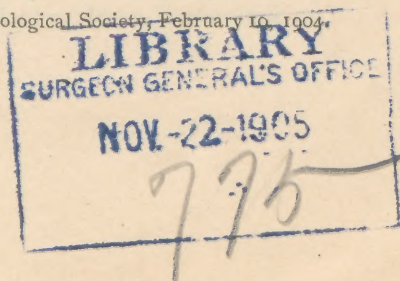
Three years ago we undertook to study the bacteriology of the blood in cases of typhoid fever entering the wards of the Second Medical Division of Bellevue Hospital. Having records of 60 cases and having collected 544 others from the literature, giving a total of 604 cases, we feel justified in making a detailed study of the results that have been obtained.

We wish to express our thanks to Professors Thompson, Loomis and Dana for placing cases at our disposal.

The presence of typhoid bacilli in the blood of typhoid cases has been suspected for many years, but only recently has the search for them proved successful.

Burdach gives a summary of the blood examinations in typhoid fever, but has collected only the German and Italian cases, ignoring the American and French. The earlier attempts, 1885 to 1895, were mostly made with small quantities of blood taken from the finger tip and, as was to be expected, afforded almost uniformly negative results. Burdach mentions about 75 such cases, of which only 4 were positive. He himself studied 6 cases, taking only small quantities of blood, with negative results. The cultures from these early cases were frequently contaminated with skin cocci, and even the reported positive results must be looked upon with suspicion, since the tests for the typhoid bacillus were very imperfect, and until the introduction of the agglutination reaction no absolutely reliable one was known.

* Read at a meeting of the New York Pathological Society, February 10, 1904.



All these earlier and more or less futile attempts have therefore been left out of consideration, and we have confined ourselves to the more recent cases, dating from 1895, when large quantities of blood have been taken from a vein and the bacilli obtained have been subjected to agglutination as well as to cultural tests.

Schottmueller takes 20 c. c. of blood, or as near that amount as can be obtained, and mixes each 2-3 c. c. with 6 c. c. of agar which is then poured into a Petri dish and allowed to set. He considers agar superior to broth, since in a solid medium the bactericidal action of the blood is less effective than in a fluid, and further, by counting the colonies, an estimate of the number of bacilli per cubic centimeter of the blood can be made.

Castellani first took blood from the finger tip and had negative results in all of 12 cases. Later he took several cubic centimeters of blood from a vein and distributed it among a number of flasks, each containing 300 c. c. of broth. After adopting this procedure, he was successful in 12 of 14 cases.

Busquet also sowed the blood in flasks containing 300 c. c. of broth, putting only a few drops into each. Dealing with such high dilutions he has been extraordinarily successful, as is pointed out elsewhere.

The American investigators have for the most part made comparatively high dilutions of the blood. We must admit, however, that in our own experiments we may have failed to prove the presence of bacilli in some instances by not sufficiently diluting the blood, and shall probably in future bring our methods more into line with those of Busquet.

Our practice has been to distribute 10 c. c. of blood into four flasks, each containing 100 c. c. of broth, and to incubate at 37 degrees C. In twenty-four hours there may be turbidity, though this does not usually occur until the second and may be delayed until the third day. As soon as a flask shows turbidity, a hanging drop is made from it and, if bacilli are found, a culture on agar is taken. From the latter further cultures are taken in glucose gelatine, litmus milk, neutral red agar and other differentiating media. The culture is also tested for its agglutinating properties in an active serum, and if it responds to all the tests is considered to be true typhoid. For agglutinating tests an immunized rabbit, which reacts up to 1:5000 or so with stock

cultures, is always kept on hand, so that a sufficiency of serum for macroscopic observations can be obtained.

The rabbit is bled from the ear and 1 c. c. of clear serum mixed with salt solution in varying dilutions, usually 1:50, 1:200 1:1000. One cubic centimeter of the dilution is pipetted into a small test tube and 1 c. c. of the culture in broth is added, making the test dilutions 1:100, 1:400, 1:2000. The tubes are put in the incubator and observations taken in one, two and three hours. If there is no reaction in three hours, the tests are considered negative. As soon as clumps visible to the naked eye are formed the reaction is marked +. When there is a distinct deposit at the bottom of the tube, but the fluid above is only partially clear, ++, and +++ as soon as the clumps have all subsided, leaving the fluid perfectly clear. When first isolated the bacilli as a rule do not agglutinate readily and may not show the reaction at higher dilutions than 1:100. It has been found by experience, however, that a clear reaction at 1:100 is sufficient for diagnosis and may be relied upon.

From the bacteriological point of view, a few specially interesting points have been brought out in the course of this study:

1. We are able to confirm the observations of others, that when first isolated typhoid bacilli react less readily to immune serum than they do later on, after having grown on artificial media.

2. There are some, however, which are specially refractory and this characteristic is often quite persistent, so that it may take several months of artificial culture before they will agglutinate readily.

3. The serum of rabbits immunized to such refractory strains quickly acquires agglutinating powers, but does not agglutinate its own strain any better than serum obtained by immunization with a strain which readily agglutinates. In other words, a good agglutinator will always agglutinate well, and a bad, badly, with any immune serum, no matter how it may have been obtained.

In our first cases, we used an apparatus devised by Dr. W. B. James for drawing the blood, consisting of a glass pipette, fitted at one end with a needle and at the other with a piece of rubber tubing for making suction. But we abandoned this in favor of the Ermold antitoxin syringe, which we find much easier to handle and quite as easily sterilized.

To show at a glance the recorded cases, with their results, we give the following summary in tabular form. Believing, as we do, that paratyphoid infections should be considered clinically as cases of typhoid fever, we have included in our totals the cases of so-called paratyphoid fever in which bacilli have been found in the blood:

TABLE OF ALL CASES REPORTED.

NUMBER.	NUMBER OF CASES EXAMINED.	BACILLUS ISOLATED.	AUTHORS.
1.....	32	20	Ruediger.
2.....	14	1	Fox.
3.....	1	1	Warfield.
4.....	2	2	Stacey.
5.....	1	0	Pratt.
6.....	15	11	Cole.
7.....	25	21	Hewlett.
8.....	3	2	Johnston.
9.....	1	1	Gwyn.
10.....	2	2	Longcope.
11.....	2	1	Allen.
12.....	3	3	Hektoen.
13.....	1	1	Jochmann.
14.....	60	34	Buxton and Coleman.
15.....	25	17	Widal.
16.....	83	83	Busquet.
17.....	37	37	Courmont and Lesieur.
18.....	1	1	Brion and Kayser.
19.....	7	7	Troussaint.
20.....	119	98	Schottmueller.
21.....	6	4	Rodhain.
22.....	56	31	Kerr and Harris.
23.....	14	11	Castellani.
24.....	3	3	Koelzer.

NUMBER.	NUMBER OF CASES EXAMINED.	BACILLUS ISOLATED.	AUTHORS.
25.....	21	9	Kuehnau.
26.....	1	1	Thiemisch.
27.....	1	1	Tiessier.
28... ..	2	2	Stern.
29.....	1	1	Sabrazes and Hugon.
30.....	1	1	Block.
31.....	2	2	Ferre and Antony.
32.....	2	2	Grandmaison et Cartier.
33.....	10	7	Auerbach and Unger.
34.....	2	2	Smith.
35.....	48	33	Warfield.
Totals.....	604	453	

The table shows the large proportion of 75 per cent. of 604 cases with bacilli in the blood at some stage of the disease, and we feel inclined to regard even this as somewhat lower than may be expected in future investigations, since the most recent records, those of Busquet and Courmont and Lesieur, show that with the most improved methods the bacilli are practically uniformly present in the first three weeks of the disease.

For the sake of completeness from the bacteriological point of view, we give a separate table of cases in which paratyphoid bacilli have been obtained from the blood.

TABLE OF CASES SHOWING PARATYPHOID BACILLI IN THE BLOOD.

NUMBER.	DAY OF DISEASE.	DAY OF RELAPSE.	BACILLUS IN BLOOD.	AUTHORS.
1.....	14	..	+	Ruediger.
	20	..	—	
	26	..	—	
	38	..	—	
2.....	13	..	+	
	20	..	—	
	27	..	—	
3.....	21?	..	—	Pratt.
4.....	11	..	—	Hewlett.
	..	4	+	
	..	10	—	
5.....	23	..	+	Johnston.
6.....	7	..	+	
7.....	10	..	—	
8.....	24	..	+	Gwyn.
9.....	10	..	+	Longcope.
10.....	15	..	+	
11.....	11	..	+	Allen.
12.....	14	..	—	
13.....	15	..	+	
14.....	5	..	+	Coleman and Buxton.
15.....	2	..	?	Brion and Kayser.
	7	..	+	
16.....	8	..	+	Schottmueller.
17.....	15	..	+	
18.....	5	..	+	
19.....	8	..	+	
20.....	21	..	+	

NUMBER.	DAY OF DISEASE.	DAY OF RELAPSE.	BACILLUS IN BLOOD.	AUTHORS.
21.....	14	..	+	Smith.
22.....	?	..	+	
23.....	?	..	+	

Some authors do not give the day of the disease on which the cultures were taken, so that the following study of the presence of the bacilli in the blood by week does not include all cases in the previous table. Further, many of the cases have been examined more than once, and in such instances each examination has been counted separately.

1. *Frequency in the first week.*

Eighty-five examinations have been made in the first week of the disease with positive results in 79, or 93 per cent. The earliest recorded positive result was obtained by Ruediger on the third day of the disease. Busquet and Troussaint report positive results on the fourth day, and a number of authors have found the bacillus on the fifth day of the disease.

2. *Frequency in the second week.*

One hundred and ninety-eight examinations have been made in the second week of the disease with positive results in 151, or 76 per cent.

3. *Frequency in the third week.*

One hundred and fifteen examinations have been made in the third week of the disease with positive results in 65, or 56.52 per cent.

4. *Frequency in the fourth week.*

Fifty-five examinations have been made in the fourth week of the disease with positive results in 18, or 32.72 per cent.

5. *Frequency after the fourth week, exclusive of relapses.*

Thirty-seven examinations have been made after the fourth week of the disease with positive results in 11, or 29.72 per cent.

The interesting fact brought out by this analysis is the large percentage of positive results obtained in the first week of typhoid fever, with the steady decline thereafter. It would appear from this that in typhoid fever the earliest and principal seat of infection is the blood, and that the disease may in truth be regarded as a septicemia. If this be true, we may in passing call attention to the utter futility of attempting to control typhoid fever by the administration of intestinal antiseptics. Of course this does not apply to the absorption of toxins other than typhoidal from and through the intestinal ulcers after these have formed.

We feel that the percentages in and after the fourth week, respectively 32.7 and 29.72, do not accurately represent the duration of life of the bacillus in the blood in the usual case of typhoid fever. In the first place, the cases are too few on which to base reliable conclusions, and in the second, the clinical course of the disease is unknown in practically all of them. Seventeen of our examinations were made on the 21st day or later, and in only three of them was the bacillus found. This, in a measure, accounts for the low percentage of positive results in our sixty cases. Courmont's experience agrees with ours in this regard. He believes that the bacilli disappear from the blood about the twentieth day. The convalescents we have examined did not show the presence of the bacillus in the blood. In the few cases where the clinical course is mentioned in the reports, the disease is marked as "severe," but the duration is not given. It is probable, however, that the examination of the blood was made in these cases for the very reason that the fever continued beyond the third week. Looked at from this point of view, the high percentages in and after the fourth week give an important clue to the unusual duration of the disease, and are as valuable in demonstrating the blood to be the principal seat of infection as the positive results in the earlier weeks.

The relation of relapses to the bacillemia is of such importance that a table of all the relapses which have been studied may be given. The interesting fact is brought out that in all but three of twenty-one relapses, or 86 per cent., the bacillus was found in the blood, indicating its reappearance. Here again, however, the number of cases is too small to attempt to draw reliable conclusions:

TABLE OF RELAPSES.

NUMBER.	DAY OF RELAPSE.	BACILLUS IN BLOOD.	AUTHORS.
1.....	3	+	Ruediger.
	16	—	
2.....	10	+	
3... ..	39 of disease	+	
	45 “	—	
4.....	6	+	Warfield.
5.....	5	+	Hewlett.
6.....	3	+	
7.....	4	+	
8.....	4	+	Hewlett's paratyphoid.
	10	—	
9.....	8	+	Coleman and Buxton.
10.....	10	—	+ In original attack.
11.....	4	+	Rodhain.
12.....	?	+	Kerr and Harris.
13.....	?	+	Auerbach and Unger.
14.....	?	+	
15.....	?	+	Schottmueller.
16.....	3	—	Kuehnau.
17.....	?	—	Courmont and Lesieur.
18.....	?	+	
19.....	?	+	
20.....	8	+	Warfield.
21.....	10?	+	

Relation of Serum Reaction to the Bacillemia.

In 73 of the 604 cases, or 10 per cent., the bacillus was present in the blood before the serum reaction was obtained. This does not include the paratyphoid infections and must be regarded as lower than the actual percentage since in the majority of cases this reaction is not mentioned.

In the light of the knowledge which this study throws upon the subject, it would seem likely on *a priori* grounds that the bacillus is always present in the blood before the serum reaction develops. The typhoid bacillus produces soluble toxins in small quantity only; the toxins are liberated from the bodies of dead bacilli. Therefore, bacilli must invade the body and be in part destroyed before the anti-bodies and agglutinins can be formed. As is well known, the serum reaction does not appear till the end of the first or in the second week of the disease, yet, as has been pointed out, the blood is already swarming with bacilli. And in many instances the serum reaction does not develop till much later than the second week.

During the past two years we have had several applications for cultures of paratyphoid bacilli to test on cases of suspected typhoid with a negative Widal reaction. So far as we have heard the tests with the paratyphoid have been uniformly unsuccessful. In several of our own cases we have been inclined to suspect paratyphoid infection on account of the absence of Widal reaction, but bacteriological examination of the blood has shown the presence of true typhoid bacilli. In such instances the serum reaction to typhoid may not be positive before the twentieth to thirtieth days, and in one of our cases did not appear until the seventy-first day. We may also mention that Professor Thompson, in the fall of 1902, observing that several of his typhoid cases at the Presbyterian Hospital did not respond to the Widal reaction, asked one of us to make bacteriological examinations of the blood for him, as he suspected paratyphoid infection. Eight such cases were tested, two with negative results, whilst from six true typhoid bacilli were isolated. Professor Thompson has kindly permitted us to use these cases for the purposes of this article.

From these observations it would certainly appear that the absence of the Widal reaction, even to the third or fourth week of the disease, by no means implies that the illness is not typhoid or that the infection is due to paratyphoid bacilli. In such cases

only a bacteriological examination of the blood can clear up the diagnosis.

The Diagnostic Value of Bacteriological Examinations of the Blood in Typhoid Fever.

In the average case of typhoid fever, neither the agglutination reaction nor a bacteriological examination of the blood is necessary to the diagnosis. Typhoid fever was recognized long before either of these tests became known, and it is probable that except in large centres or university towns that the great majority of cases are diagnosed, and correctly, to-day without these aids. The serum reaction may be obtained with dried blood or blood serum in a capillary tube sent to a distance, but a bacteriological examination of the blood demands not only complete laboratory facilities, but an experienced bacteriologist. Therefore we feel skeptical as to the general application of this aid to diagnosis. Yet the bacteriological diagnosis of typhoid fever is a distinct advance. It finds its applicability in just those cases where the clinical phenomena and even the serum reaction fail us, and, if future studies confirm the uniformly successful results of Busquet and Courmont and Lesieur, many doubtful cases may be cleared up. We think that little objection to the procedure need be apprehended on the part of the patients themselves or the patients' families, for in the majority of cases it is very simple and, by using ethyl chloride, may be accomplished practically without discomfort. However, as said above, it will be the exceptional case in which a bacteriological diagnosis will become necessary.

May the Colon Bacillus Cause a Primary Systemic Infection?

Since in two of our cases, Nos. 34 and 35, marked as negative in the tables, we found the bacillus coli communis in pure culture, the important question arises whether this organism is capable of causing a primary systemic infection, or whether its occasional presence in the blood is to be regarded as a secondary invasion. In the literature we have been able to find only one similar case. Fox, in 14 examinations of the blood, isolated the typhoid bacillus from one and the colon bacillus from another. Since there were several colonies of the latter in pure culture on his agar plates, it does not appear probable that their presence was due to accidental contamination. In this instance the serum of the patient became positive to Widal on the thirty-second day, though it had previously been negative, so that there may have been a mixed infection.

Under the title of Colon Bacillus Infection, Burch reported, in 1902, a series of cases presenting typhoidal symptoms which lasted from 7 to 10 days. The Widal reaction was negative (dilution not stated) in every case throughout its course. In many of the cases the urine was turbid and swarmed with motile bacilli which responded to the cultural tests for *B. Coli communis*. The sera of the patients uniformly gave a complete reaction with the bacilli obtained from the urine, but here again the important fact of the degree of dilution is not stated.

Evans and Sailer, of Philadelphia, likewise mention a case of apparent typhoid where the serum in the third week was positive at 1:150 with a culture of *coli communis* obtained from Paris, but only gave an imperfect reaction with typhoid at 1:10. No blood cultures were taken, but it seems likely that this was an instance of colon infection.

In case 34 of our series the colon bacillus was found in the blood on the eighth day of the disease, the serum reaction against typhoid having been negative on the sixth day. As, however, the reaction became positive on the ninth day, the presence of the colon bacillus must be regarded as part of a mixed or secondary infection. The case ran a very mild course.

In case 35 the colon bacillus was found on the tenth day and the serum reaction against typhoid was negative as late as the twelfth. This case also was exceedingly mild and was of short duration. Unfortunately, owing to vacations, the bacillus was not identified as *coli communis* until the case had left the hospital, so that its bearing on the question of systemic colon infection, while suggestive, was not determined.

In order to make our own cases available for future statistical studies, we append the following table, giving the more essential facts concerning them:

NUMBER.	DAY OF DISEASE.	DAY OF RELAPSE.	BACILLUS IN BLOOD.	SERUM REACTION.	REMARKS.
1.....	21	..	—	+	
2.....	40	..	—	+	Convalescent.
3.....	..	8	+	..	Relapse.
4.....	14	..	+	—	
5.....	21	..	—	—	
6.....	60	..	—	+	Convalescent.
7.....	5	..	+	—	Paratyphoid.
	27	..	—	..	
8.....	14	..	+	..	
9.....	28	..	—	+	
10.....	21	..	—	—	Diagnosis doubtful.
11.....	14	..	—	+	
	19	..	—	..	
12.....	8	..	+	—	
	20	..	+	..	} Serum reaction + with own bacillus, 1:80.
13.....	8	..	—	—	
	13	..	—	..	Blood clotted in tube.
	19	..	—	..	
	27	..	+	+	
14.....	14	..	+	+	
15.....	14	..	—	+	
16.....	8	..	+	+	
17.....	14	..	+	+	
18.....	14	..	+	+	
19.....	8	..	—	..	
	13	..	+	..	Agglutinates badly.
20.....	11	..	—	—	
21.....	11	..	—	+	
22.....	8	..	+	+	Agglutinates badly.
23.....	21	..	+	+	

NUMBER.	DAY OF DISEASE.	DAY OF RELAPSE.	BACILLUS IN BLOOD.	SERUM REACTION.	REMARKS.
24.....	14	..	—	..	
	21	..	—	..	
25	14	..	—	—	
26.....	14	..	+	—	
		10	—	..	Relapse.
27.....	14	..	+	—	
28.....	8	.	+	—	
29.....	—	..	
30.....	—	+	
31.....	—	..	
32.....	11	..	+	+	
33.....	9	..	+	+	
34.....	8	..	—	..	Colon bacillus.
35.....	10	..	—	..	“ “
36.....	8	..	+	+	
37.....	8	..	—	—	
	25	..	—	..	Serum reaction + 35th day.
38.....	12	..	+	+	
39.....	38	..	—	—	} Serum reaction + 71st day (Dr. Dow's case).
40.....	14	..	+	—	
41.....	13	..	+	+	
42.....	12	..	—	+	
	14	.	+	+	
43.....	10	..	—	+	
44.....	8	..	+	—	
45.....	7	..	+	—	Dr. Nammack's case.
46.....	26	..	—	—	“ “ “
47.....	10	..	+	+	
48.....	10	..	+	—	
49.....	8		+	—	

NUMBER.	DAY OF DISEASE.	DAY OF RELAPSE.	BACILLUS IN BLOOD.	SERUM REACTION.	REMARKS.
50.....	23	..	—	+	
51.....	11	..	—	—	
52.....	19	..	+	—	Dr. Thompson's Presbyterian Hospital case. Dr. Thompson's Presbyterian Hospital case. Dr. Thompson's Presbyterian Hospital case. Dr. Thompson's Presbyterian Hospital case. Dr. Thompson's Presbyterian Hospital case. Dr. Thompson's Presbyterian Hospital case. Dr. Thompson's Presbyterian Hospital case. Dr. Thompson's Presbyterian Hospital case.
53.....	29	..	—	—	
54.....	7	..	+	—	
55.....	21	..	—	—	
56.....	9	..	+	—	
57.....	21	..	+	—	
58.....	16	..	+	—	
59.....	11	..	+	—	
60.....	10	..	—	..	

In conclusion, we wish to express our indebtedness to Dr. Letchworth Smith for his kindness in isolating the bacilli in a number of cases.

BIBLIOGRAPHY.

- Ruediger.....Medicine, Detroit, 1903; 9, 258.
 FoxProc. Path. Soc. Philadelphia, 1902-3; n. s. 6
 185.
 WarfieldJohns Hopkins Hospital Bull., 1902; 13, 173.
 StaceyAustralasian Med. Gaz., 1902; 21, 504.
 PrattBoston M. and S. Journ., 1903; 148, 137.
 ColeJohns Hopkins Hospital Bull., 1901; 12, 203.
 HewlettMedical Record, 1901; 60, 849.
 ———Am. Journ. Med. Sci., 1902; 124, 200.
 JohnstonAm. Journ. Med. Sci., 1902; 124, 187.
 GwynJohns Hopkins Hospital Bull., 1898; 9, 54.
 LongcopeAm. Journ. Med. Sci., 1902; 124, 209.
 AllenAm. Journ. Med. Sci., 1903; 125, 96.
 HektoenMedical News, 1903; 83, 580.
 JochmannCentralbl. f. Bakt. Referate, 1903; 33, 8-9.
 Coleman and BuxtonAm. Journ. Med. Sci., 1902; 123, 976.
 WidalLa Méd. Mod., 1902; 13, 407, Discussion.
 BusquetLa Presse Méd., 1902; 101, 54, 593.
 Courmont et Lesieur.....Journ. de Phys. et Path. gen., 1903; 5, 32.
 Brion and Kayser.....Münch Med. Woch., 1902; No. 15, 611.
 TroussaintLa Méd. mod., 1903; 14, 44.
 SchottmuellerMünch Med. Woch., 1902; p. 720.
 RodhainBull. Acad. Roy. de Méd. de Belg., Bruxelles,
 1903; 4s., 17, 309.
 Kerr and Harris.....Chicago Medical Recorder, 1902; 23, 232.
 CastellaniCentralbl. f. Bakt. I. Orig., 1902; 31, 477.
 KoelzerZeitschr. f. Hygiene, 1901; 36, 75.
 KuehnauZeitschr. f. Hygiene, 1900; 25, 354.
 ThiemischInaug. Diss. Bresslau, 1894; ref. Centralbl. f.
 Bakt., 1895; 17, 475.
 TeissierArch. de Méd. Expér., 1895; 7, 660.
 SternCentralbl. f. inn. med., 1896.
 Sabrazes and HugonSoc. Med. des. Hôp., 1897; 3s., 14, 19.
 BlockJohns Hopkins Hospital Bull., 1897; 8, 119.
 Ferre and AntonyJ. de Méd. de Bordeaux, 1897; 27, 369.
 Grandmaison and Cartier ..Soc. de Biol., 1899; pp. 56, 862.
 Auerbach and Unger.....Deutsch Med. Woch., 1900; p. 76.
 SmithJourn. Am. Med. Assn., 1903; 41, 1470.
 BurchN. Y. Med. Jour., 1902; 75, 938.
 Evans and SailerUniv. Penn. Med. Bull., 1903; 16, 138.
 BurdachZeitschr. f. Hygiene, 1902; 41, 305.
 WarfieldBull. Ayer Clin. Laby. of Penn. Hospital; I,
 October, 1903.

